Early Journal Content on JSTOR, Free to Anyone in the World

This article is one of nearly 500,000 scholarly works digitized and made freely available to everyone in the world by JSTOR.

Known as the Early Journal Content, this set of works include research articles, news, letters, and other writings published in more than 200 of the oldest leading academic journals. The works date from the mid-seventeenth to the early twentieth centuries.

We encourage people to read and share the Early Journal Content openly and to tell others that this resource exists. People may post this content online or redistribute in any way for non-commercial purposes.

Read more about Early Journal Content at http://about.jstor.org/participate-jstor/individuals/early-journal-content.

JSTOR is a digital library of academic journals, books, and primary source objects. JSTOR helps people discover, use, and build upon a wide range of content through a powerful research and teaching platform, and preserves this content for future generations. JSTOR is part of ITHAKA, a not-for-profit organization that also includes Ithaka S+R and Portico. For more information about JSTOR, please contact support@jstor.org.

GENERALIZED BLASTOMYCOSIS.

REPORT OF A CASE WITH MILIARY AND ULCERATIVE BLASTOMYCOSIS OF THE LUNGS; MILIARY BLASTOMYCOSIS OF THE SPLEEN; AND MULTIPLE SUPERFICIAL AND DEEP ABSCESSES.*

E. E. IRONS AND E. A. GRAHAM.

(From the Surgical Clinic of Dr. D. W. Graham and the Pathological Laboratory, Rush Medical College, Chicago.)

IT is now known that infection with certain members of the group Oidium may become disseminated throughout the human body, and *generalized blastomycosis* or *oidiomycosis* must be recognized as a clinical entity. Several cases have been reported, including five from Chicago, but until recently certain observers, particularly among the Germans, have been inclined to doubt the statement that blastomyces was the sole etiological factor in some at least of the cases reported. The present case † presents several points of clinical and pathological interest, and in reporting it somewhat at length it is hoped that something may be added to our knowledge of the clinical course and pathology of the disease.[1]

THE CLINICAL HISTORY.

A. D., age 47, German, lumberman. Admitted to the Presbyterian Hospital September 11, 1905.

The family history is negative as to tuberculosis and malignant diseases. A wife and two children are living and well; no history of miscarriages. The patient had typhoid fever 14 years ago. Otherwise has had no severe illness until the present. Denies all venereal infection. Has never suffered from sore throat, alopecia, nor eruption of any kind until the present lesions appeared. Has taken alcohol in small amounts. Has lived in Chicago for a number of years working in a lumberyard until obliged to give up work on account of the present trouble.

In March, 1905, the patient noticed a small subcutaneous nodule on the inner surface of the right thigh about five inches below Ponpart's ligament. This nodule was slightly tender, and gradually increased in size to that of a small hen's egg, softened, and finally broke through the skin with the discharge of bloody pus, leaving an ulcer

---

* Received for publication June 1, 1906.

† The case was demonstrated from time to time in the clinic by Doctor Graham, to whom we are indebted for the opportunity of studying the clinical course of the disease.

[1] For bibliographies reference may be made to the following articles: RICKETTS, *Jour. Med. Res.* 1901, 1, p. 373; BUSCHKE, *Bibliotheca Medica*, Stuttgart, 1902, Abtheil. 2, Heft 10; BASSOE, *Jour. Infec Dis.*, 1906, 3, p. 91.

which healed slowly with the formation of a slightly indurated reddish-brown scar. Previous to the appearance of this lesion there had been no cutaneous lesions on any part of the body.

Before the first lesion on the thigh had healed a second appeared on the forehead and then other similar lesions on the legs, hips, and arms, in rapid succession, all of which ran a course similar to that of the first, unless incised, in which case healing was slightly more rapid.

The constitutional symptoms which were relatively slight at first, became more marked, and about six weeks after the onset, the patient was confined to his room, largely on account of weakness, but undoubtedly partly by reason of the unsightly appearance of the lesions on his face and arms, in regard to which he was very sensitive, having been told by his physician that they were of syphilitic origin.

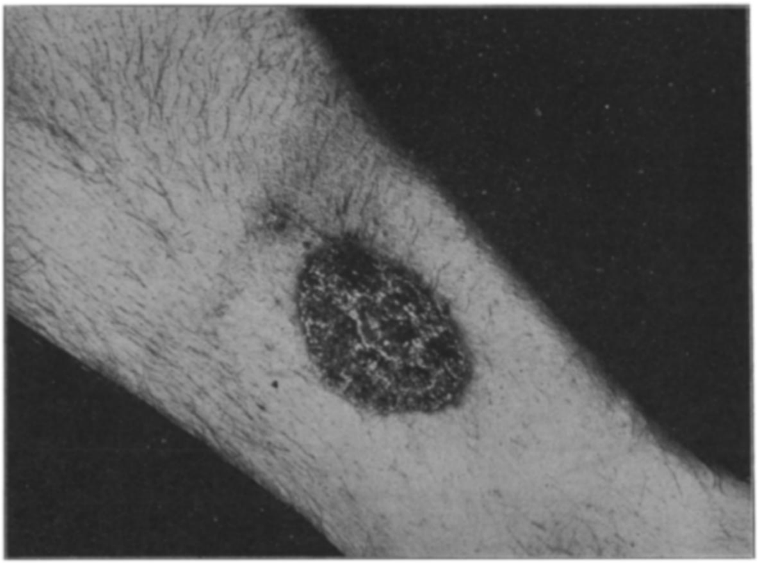


FIG. 1.—Old, partially healed ulcer of the leg present on admission to the hospital.

The chief symptoms at this time were weakness, anorexia. and slight fever. Previous to admission to the hospital there was no cough or other pulmonary difficulty. Physicians who had seen him up to this time were divided in their diagnoses between syphilis and tuberculosis.

Two months after the appearance of the first lesion, the right and then the left ankle became swollen, painful, and slightly reddened. Lesions over the malleoli similar to the others appeared soon after, but they did not heal so rapidly, and on admission to the hospital six months after the appearance of the first nodule on the thigh, both ankles were considerably swollen, red, and tender, so that it was almost impossible for the patient to stand, on account of the pain produced.

Examination on admission.—The patient is a middle-aged man, medium height, rather poorly nourished, and shows a marked anemia. There are several slightly indurated scars over the forehead. The eyes, ears, and nose are normal; tongue coated; pharynx normal. There are several hard pea-sized glands in the posterior triangles of the neck. Heart and lungs are negative. Abdomen and genitalia normal. At various points over the body are lesions in all stages of development.

Scars of healed and partially healed lesions over the forehead, right forearm, both hips, thighs, and legs (Fig. 1). Fluctuating abscesses over both elbows (Fig. 2), left forearm, left patella, right heel, left external malleolus. Both ankles are swollen, painful, tender on pressure, dull red in color, and slightly edematous. There is some limitation of motion, though this seems to be due largely to periarticular swelling and tenderness.

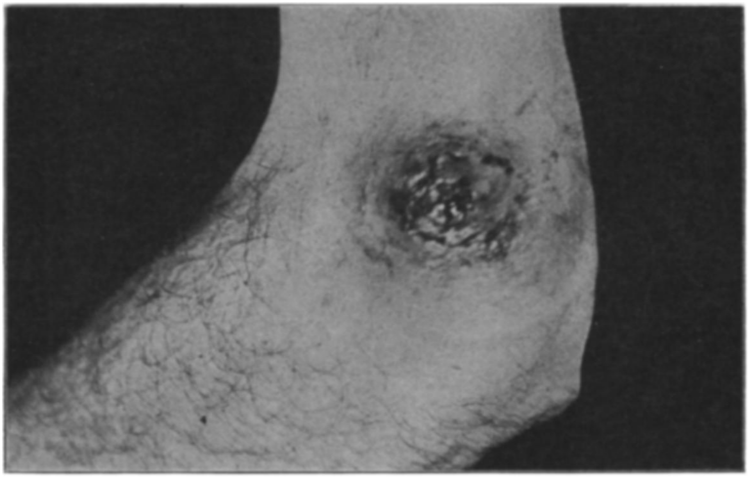


FIG. 2.—Subcutaneous abscess which has discharged spontaneously by erosion of the overlying skin.

The more superficial lesions begin as small, hard, subcutaneous nodules, gradually enlarging, with some tenderness. They soon become soft, fluctuate, and, if not incised, break through the skin with the discharge of reddish bloody pus in which can be demonstrated yeastlike, budding organisms, often in immense numbers. Other abscesses are deeply seated, some of them being subperiosteal in origin. In the deeper lesions there is a tendency to extensive dissection along the intermuscular fasciæ after the manner of tuberculous abscesses.

The superficial lesions present on admission, said by the patient to have followed abscesses, present a roughly oval outline, edges fairly regular and slightly raised, with occasional though rare miliary abscesses, such as are found in the ordinary lesions of blastomycetic dermatitis. In none of these miliary abscesses is it possible to demonstrate the organisms. Surrounding each ulcer is a dark red, often purplish zone. The ulcer has a rather irregular floor formed by granulation tissue, with here and there processes of newly-formed epidermis extending inward from the margins. The whole is covered by a dry, rather firmly attached, horny crust. The ulcers show no tendency to progress, and the healing though slow is continuous. The scars are reddish-brown, occasionally indurated, but in general slight in comparison with the extent of the original lesions.

Those ulcers which followed abscesses developing while in the hospital showed several points of difference from the foregoing, due to the treatment. Instead of being allowed to enlarge until spontaneous evacuation by erosion of the skin occurred, the abscesses were incised and the pus evacuated as soon as fluctuation could be demonstrated. The initial damage to the skin and subcutaneous tissue was thus much decreased, and the lesions remained as freely discharging superficial abscesses, which healed fairly rapidly up to the last few months of illness, when there was evident a tendency to sloughing of the subcutaneous tissue with undermining of the skin.

Course.—After a few days' rest in bed the swelling and redness of the ankles decreased. Two abscesses over the malleoli were drained, and denuded bone found. The patient was allowed up in a wheel chair, which he used almost daily up to the day of his death.

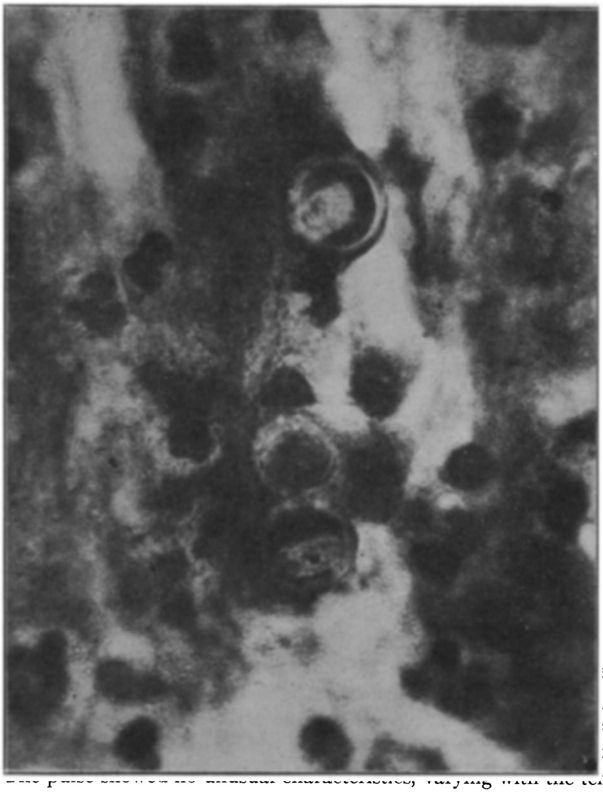
The lungs at the time of admission (September 11) were normal on physical examination. There was no cough or other pulmonary symptoms. On September 25 the patient for the first time had a slight cough and complained of some pain in the left side. Examination showed slight dulness and harsh breath sounds, together with a few fine moist râles in the left infraclavicular and midscapular regions. No friction could be demonstrated. The remaining chest area was normal, and there was no coincident change in constitutional symptoms. The expectoration was small in amount and mucopurulent. Repeated examinations failed to show blastomycetes or tubercle bacilli.

Two weeks later the cough and pain had disappeared and aside from slight relative dulness in the left midscapular region, the chest findings were normal.

On November 6 the general condition of the patient was less favorable. The cough and pain in the chest reappeared. Examination showed dulness and râles in both infraclavicular fossæ. Posteriorly in the midscapular region on both sides were signs of consolidation, more marked on the left side. The expectoration was mucopurulent, moderate in amount, and on examination showed large numbers of blastomycetes. These were easily demonstrated in fresh specimens of sputum mounted in 1 per cent potassium hydrate, and also in coverslip preparations stained with methylene blue, and hematoxylin and eosin (Fig. 3). No mycelial threads were found. The sputum was again repeatedly examined for tubercle bacilli, with negative results. The relative absence of secondary infection was a noticeable characteristic of the sputum at this time, which consisted almost entirely of mucus, leucocytes, epithelial cells, and the budding organisms. With the extension of the disease in the lungs the sputum increased in quantity to about 125 c.c. in 24 hours, and occasionally small amounts of blood appeared intimately mixed with the mucopurulent secretion. Active hemorrhage did not occur.

From this time on the patient grew steadily weaker. New lesions appeared in rapid succession over the body, particularly involving the extremities and head, and with the decline in general condition healed correspondingly more slowly. At several points including the left malar and left frontal bones, right patella, and right external malleolus denuded bone could be demonstrated.

During the last three weeks of life there was marked destruction of the subcutaneous tissue at the sites of the lesions, so that relatively large areas of skin were undermined in spite of the employment of free drainage. A large abscess which formed over the right hip sloughed extensively a few days before death. There were no signs or symptoms of invasion of the vertebræ. On the day of death the patient became rapidly worse, with some elevation of temperature, rapid pulse, and delirium, presumably



due to an 18, 1906,
10 months
The t spital was
irregular, ening. At
other time uently the
increase in ss, though
this was n companied
by chills. nperature,

though during the last three months of illness the average pulse-rate was relatively increased.

Blood.—On admission (September 11) the blood count showed 16,000 leucocytes per c.mm.

On October 15 a blood examination showed the following:

Erythrocytes	4,320,000
Leucocytes	12,500
Hemoglobin (Dare)	45%

A differential count of 250 leucocytes showed—

Polynuclear neutrophiles.	75.6%
Large mononuclears	7.6
Small mononuclears	10.8
Indentate nucleus	2.0
Eosinophiles	3.2
Myelocytes	0.8

The red cells were pale and averaged rather smaller in size than normal. No nucleated forms were found. There was slight polychromasia present.

A third blood examination on December 15 gave the following:

Erythrocytes	4,160,000
Leucocytes	21,200
Hemoglobin (v Fleishl)	55%

At this time the patient was markedly emaciated and more anemic in appearance than on admission. There was also a secondary staphylococcus infection of two abscesses when this count was made.

A differential leucocyte count showed—

Polynuclear neutrophiles	93.2%
Large mononuclears	3.2
Small mononuclears	2.8
Eosinophiles	0.8

There were slight poikilocytosis and polychromasia, but no nucleated reds were found.

Blood cultures.—Blood cultures were made on two occasions (December 15 and December 30), using various media including blood serum, glycerin, glucose-agar slants, broth tubes and flasks, and glucose-agar plates. The cultures were sterile throughout.

Urine.—The urine on admission was yellow, clear, acid, and showed a trace of albumen; no sugar. A few hyalin and finely granular casts were found in the centrifugalized specimen. A 24-hour specimen of 1,625 c.c. had a specific gravity of 1,015 with a trace of serum albumen; no sugar. In the sediment were occasional hyalin and finely granular casts and a few leucocytes. Several subsequent examinations up to within a few days of death gave practically the same results. At no time were blastomycetes found in the urine, although careful search was repeatedly made in view of the renal involvement reported in some other cases of generalized blastomycosis.

Feces.—The bowels were practically normal throughout the illness. There was no diarrhea and the feces were normal in appearance.

Treatment.—The abscesses as they appeared were incised and drained, with subsequent daily dressings. To some of the abscesses a 1 per cent aqueous solution of copper sulphate was applied, while others were treated with plain sterile gauze.

During the first month of this treatment, the lesions on which the copper sulphate was used healed somewhat more rapidly than the others, but owing to the rapid decline in the general condition of the patient from this time on, any further comparison of the methods would be only misleading. The copper sulphate did, however, materially reduce the tendency to secondary infection, and it was subsequently used on all abscesses. It is worthy of note that with numerous lesions over all the extremities, the dressings of which occasionally were unavoidably displaced by the movements of the patient, there was practically no infection with ordinary pyogenic organisms. Certain of the superficial lesions present on admission were treated with the X ray with no marked benefit.

Internally in addition to full diet and general tonic treatment, the patient was given potassium iodide in increasing doses up to 60 grains per day. For a time also he received copper sulphate gr. $\frac{1}{8}$ three times a day, but after a short time this was discontinued on account of gastrointestinal disturbance.

Cultural and animal experiments with materials obtained during life.—The pus from the abscesses was of a bloody, fluid character, consisting of blood cells, pus cells, tissue debris, and the organisms, often in large numbers. Only the yeastlike forms were found in the pus. These were easily demonstrated in the fresh preparations mounted in 1 per cent potassium hydrate.

Although the organisms occurred in pure culture and often in large numbers in the abscesses, considerable difficulty was experienced in obtaining growths on artificial media. For example, of six complete series of cultures on various media, including broth, glucose agar, glycerin agar, and blood serum, in only two series were growths obtained, and in these the growths occurred on practically all the media employed. Inasmuch as there were no recognizable differences in the media of the several series, it would appear that certain variations occur from time to time in the ability of the organisms to withstand the change of environment entailed in the transfer from the tissues to artificial media. Having once obtained growths on artificial media, no difficulty was experienced in maintaining them.

The organisms were obtained in pure culture from abcesses on the forearm and on the patella, and also on one occasion from the sputum.

With a view to excluding the tubercle bacillus as a possible factor in the disease, pus from the abscesses was inoculated intraperitoneally and subcutaneously into guinea-pigs, and the animals examined from three to six weeks later. No trace of tuberculous infection could be found in any of these animals. As already stated, many preparations from the pus and sputum were stained for tubercle bacilli with negative results.

THE NECROPSY RECORD.

The necropsy was performed six hours after death by Dr. E. R. LeCount.

Anatomical diagnosis.—Miliary blastomycosis of lungs and spleen; ulcerative blastomycosis of the upper lobe of the left lung; multiple subcutaneous abscesses and sinuses involving the face, scalp, and all the extremities; retroesophageal abscess with erosion of the bodies of the seventh cervical to the fifth dorsal vertebræ (inclusive) and the anterior surfaces of the vertebral extremities of the second to the fifth left ribs; erosion of left parietal bone; sloughing deep ulcer of right thigh; abscess of thyroid cartilage; subpleural hemorrhages of right lung; bilateral fibrous pleuritis; hyperplastic splenitis; hyperplasia of mesenteric lymph glands; brown atrophy of the heart; colloid goiter (all lobes); slight sclerosis of anterior mitral leaflet and root of aorta; chronic catarrhal gastritis; localized fibrous peritonitis; chylous ascites (slight); slight atrophy of liver; retention cysts of left kidney.

The body is that of a middle-aged, much emaciated man. Body still warm. There are small subcutaneous abscesses over the left parietal bone and in the right infraorbital region. Two slightly indurated scars over the forehead, and there is a slightly raised wartlike lesion on the right side of the nose. There are partially healed subcutaneous abscesses on the lips, left ear, and in the right submaxillary region. A large sloughing area is present on the right buttock, which connects with an abscess in the muscles of the thigh. There is also a large abscess over the right knee with extensive undermining of the skin, from which considerable thick reddish pus can be expressed. There are subcutaneous abscesses over both ankles with denudation of bone, and healed and partially healed lesions over both forearms, thighs, legs, and several of the fingers.

Abdominal wall thin, muscles are light brown and dry. There is a small amount of milky fluid in the pelvis. The appendix is free, peritoneum smooth and glistening. Old adhesions between the gall-bladder and colon. The mesenteric glands are large. The diaphragm extends to the fourth right rib and the fourth left interspace. The pericardium contains a large amount of clear fluid. There are bands of fibrous adhesions of the pleuræ.

The thyroid gland is symmetrically enlarged and weighs 65 grams. The cut surface shows an increase in colloid material and fibrous tissue.

In the covering of the thyroid cartilage on the right side there is a small cavity containing purulent material. The cartilage below appears to be normal. The larynx and trachea show no changes.

Over the upper lobe of the right lung are a number of subpleural hemorrhages. The right lung is rather dry, and the tissue filled with small nodules, miliary, or slightly larger in size, with hemorrhagic borders. The lung weighs 545 grams. The left lung shows adhesions at the apex in which are large areas of consolidation. Section shows numerous connected small cavities, 1–1.5 cm. in diameter. The lower lobe answers to the description of the right lung.

The heart is small, and weighs 225 grams. The epicardial fat is replaced by a gelatinous substance and the epicardial vessels are tortuous. The anterior leaflet of the mitral valve shows some thickening along the line of attachment of the chordæ tendineæ. The beginning of the aorta shows a few yellowish placques. The wall of the left ventricle is 15 mm. in thickness; that of the right ventricle is 4 mm. and flabby.

On removal of the pharynx and esophagus there is opened an abscess cavity posterior to the esophagus; there is erosion of the spinal column from the inferior margin of the fifth dorsal vertebra to the seventh cervical. It is more marked on the left side and extends laterally far enough to involve the anterior surfaces of the second, third, fourth, and fifth ribs. The abscess contains a small amount of yellowish pus.

The lining of the esophagus is smooth. The stomach small and empty. Stomach wall is thicker than normal and rugæ prominent and cannot be obliterated by stretching. The intestines show no changes.

The thoracic duct is patent.

The liver weighs 1,300 grams. It is smooth externally, of normal color. There is a relative increase of intralobular connective tissue, and the centers of the lobules are deep red. The gall bladder contains a considerable amount of bile.

The pancreas weighs 85 grams.

The spleen weighs 300 grams, and is firmly adherent to the diaphragm from which it can be separated only by lacerating the capsule. It cuts easily, is dark red in color, and at several points in the pulp there can be seen small whitish areas, pin-point or less in size which appear to be rather too white and prominent to be Malpighian cor puscles.

The adrenals are normal.

The kidneys weigh 320 grams, smooth externally, capsule slightly adherent, fetal lobulation is unusually well preserved; color and markings are normal. There are several minute cysts in the cortex of the right kidney.

The bladder shows no changes. The prostate is not enlarged, but contains more than the normal amount of fibrous tissue.

The brain externally and on section shows no changes.

HISTOLOGICAL EXAMINATION.

Lungs.—The nodular areas seen at the necropsy resemble miliary tubercles. If one be examined with the high power there is seen in the center a mass of necrotic

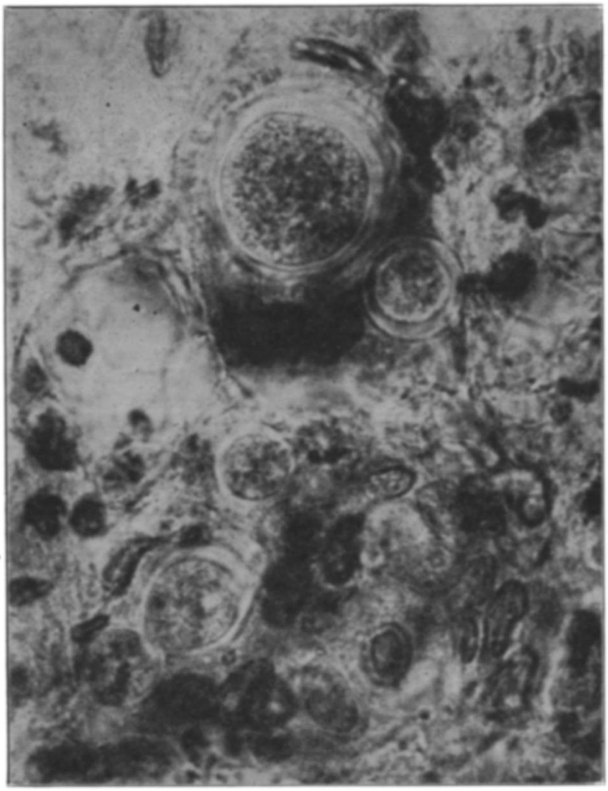


FIG. 4.—Section of lung showing several blastomycetes with characteristic double contours. Hematoxylin and eosin. Photomicrograph, × 1,500.

tissue, containing numbers of polymorphonuclear leucocytes, red corpuscles, desquamated epithelial cells, and many blastomycetes. Immediately surrounding this necrotic focus is a zone of giant cells of the Langerhans type, and embryonic connective tissue cells. As many as 15 giant cells occur in some places and almost without exception they contain blastomycetes in varying numbers. Outside is an area of small round cells with a few connective tissue fibers and distended blood capillaries. Plasma cells are occasionally found. In these areas the alveolar walls are often indistinguishable, and the bronchioles contain large numbers of desquamated epithelial cells, cellular detritus, and in a few instances two or three blastomycetes. Occasionally a bronchiole can be made out at the center of such an inflammatory focus. In the region of one of the minute abscesses a large blood vessel is seen to contain two blastomycetes. Many of the aveoli in the less affected areas contain desquamated epithelium and a cellular detritus; others are markedly emphysematous.

In general these regions of pneumonia are adjacent to the larger blood vessels and bronchioles. By the study of a number of serial sections it is seen that the condition is a true broncho-pneumonia. The inflammatory foci surround the respiratory bronchioles and increase in area toward the periphery of the lung, thus corresponding with the ramifications of the tubules. Furthermore, the alveoli situated farthest from the bronchioles are least affected.

The intima of the larger blood vessels is slightly thickened. The lymph channels contain a considerable amount of black pigment. The visceral pleura is somewhat thickened, and small areas of hemorrhage are seen beneath the endothelial layer.

Retroesophageal abscess.—Sections from the lining of the large abscess show next the abscess cavity, necrotic tissue, and polynuclear leucocytes; surrounding this is an area consisting largely of giant cells containing blastomycetes, together with fibroblasts and numbers of small round cells.

Spleen.—The small whitish, pin-point areas noted in the fresh specimen, prove to be minute collections of blastomycetes surrounded by polynuclear leucocytes and necrotic tissue. No giant cells are seen.

Kidney.—Sections show only a rather marked passive hyperemia. Numbers of sections from various portions of the organs were examined, but no abscesses nor organisms were found.

Thyroid.—Many of the alveoli in the thyroid are enlarged and there is present an excess of colloid material.

Sections from the liver, pancreas, mesenteric gland, adrenal and myocardium show no important changes. The prostrate shows a moderate increase in fibrous tissue with occasional corpora amylacea.

STUDY OF SMEARS AND CULTURES.

Cultures and smears were made of the peritoneal, cerebrospinal, and pericardial fluids, heart's blood, pus from the retroesophageal abscess and from an abscess over the right knee, and of the kidney, spleen, and liver. Coverglass preparations were also made of fluid expressed from affected portions of the left lung. Films made from the heart's blood, pericardial and peritoneal fluids showed no organisms, and cultures remained sterile for four weeks. The *Streptococcus pyogenes* was obtained in coverslip preparations and pure culture from the cerebrospinal fluid, liver, spleen, and kidney, the *Staphylococcus pyogenes aureus* was found in the liver and spleen and in pus from the retroesophageal and knee abscesses. Films prepared from the pus of the two abscesses just mentioned and from fluid expressed from the pneumonic areas in the lung showed many yeastlike organisms with budding forms, varying in size from 7 to 20 μ in diameter.* Efforts to isolate the yeast from the pus of the abscesses were unsuccessful. The organism was, however, obtained in pure culture from the kidney, although no yeast cells were found in coverslip preparations made from that organ.†

The yeastlike organism obtained postmortem agreed culturally and morphologically with the organism repeatedly isolated from the several abscesses and from the sputum during life. We experienced the same difficulty in obtaining growths from the postmortem material as from the fresh pus. In the first series of cultures growth appeared only after seven days and proceeded slowly, but after the fourth transfer on glucose agar small colonies were visible in three days at 37° C. After growth was once obtained cultures were readily maintained on all the usual laboratory media and showed no tendency to die out.

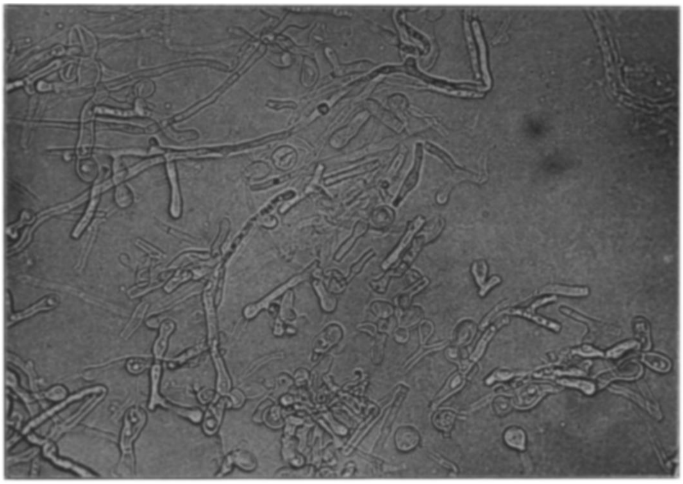


FIG. 5.—Blastomycetes from a a culture in which budding forms are prominent. Glucose agar. Mounted in per cent KOH. × 300.

Morphology.—A typical young culture on glucose agar answers to the following description: There are small white colonies which under a low-power lens are seen to possess numerous aërial hyphæ with usually single terminal and numerous lateral conidia. Coverglass preparations show many doubly contoured segmented threads with homogeneous protoplasm, except that in some of the segments there are from two to four small, spherical, highly refractile bodies about 1 μ in diameter, arranged in the midaxis of the segments. The segments vary from 16 to 29 μ in length and

---

* A careful examination of material from the lungs was made for tubercle bacilli, but none were found.

† In making cultures from the kidney, as is the routine in this laboratory, a piece of the organ removed under precautions to prevent contamination from either the air or renal pelvis was dropped into sterile broth, and macerated, and this turbid suspension used as material for the inoculation of culture media.

from 3 to 5 μ in width. At various points segments pass off at right angles to the main chain and terminate in a slightly rounded tip, similar to that of the terminal segment of the main stem. At other points in place of lateral segments there are globular structures, from 6 to 8 μ in diameter, connected with the main stem by short, doubly contoured pedicles. These globular offshoots are similar in the relations of their cell walls and protoplasm to the terminal conidia; and both structures are often seen to contain several spherical, highly refractile bodies, 0.5 to 1 μ in diameter, suggesting ascospores in appearance. Besides the hyphal and mycelial portions of the growth there occur in the cultures budding forms similar to those found in the tissues. These budding forms show a characteristic double contour and a more or less granular protoplasm. Occasionally the beginning development of the mycelial threads from one of the budding forms is observed.* (Figs. 5 and 6).

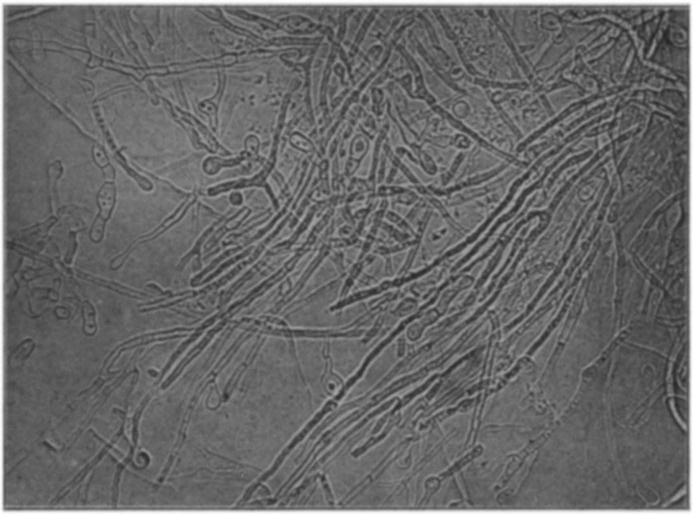


FIG. 6.—Blastomycetes from a culture in which the mycelial forms predominates. The characteristic branching, lateral budding, and protoplasmic granulation can be seen. Glucose agar. Mounted in 1 per cent KOH. × 300.

Cultures.—On *plain* and glycerin agar growths occur in from five to seven days and vary in appearance with the amount of moisture present. In relatively dry cultures the growth is moldlike, elevated, with definite margins, and of a white color from the formation of aërial hyphæ. Surrounding the elevated portion of the growth is a non-elevated rather translucent zone which microscopically is found to consist of numerous interlacing mycelial threads growing in the superficial layers of the medium. Where larger amounts of moisture are present the growth is more pasty, brownish in color, and consists almost entirely of mycelial threads. In younger cultures and in those freshly isolated a number of budding forms are found.

---

* Aërial fructification, one of the characteristics of the *oidium hyphomycoide* of Ricketts, was never observed. The proportion of budding forms to hyphæ varied with the kind of media, age of the culture and condition of environment. Lower temperatures, lack of oxygen, marked alkalinity, and the presence of much moisture seemed to favor the formation of mycelium and aërial hyphæ. In cultures in which the reverse conditions obtained budding forms were much more numerous.

On *glucose agar* the growth is more profuse with the formation of mycelium and aërial hyphæ. These hyphæ often form, after three or four weeks, a white, felt-like mass resembling a plug of cotton. Here, as in other media, the mycelia tend to grow down into the deeper layers of the medium which gradually becomes rich golden brown in color.

In *broth* (1 per cent acid to phenolphthalein) there forms a fluffy, coherent, globular growth consisting of many very long mycelia radiating out in all directions from the central point of inoculation, the supernatant liquid remaining clear.

Gelatin is not liquefied after five weeks.

Litmus milk after 10 days is slightly alkaline and proteolysis without coagulation has occurred.

On *potato* the growth is rather more rapid than on other media, and there are many aerial hyphæ. In certain of these cultures the hyphæ persist, but in others for some reason they begin after a few days to disappear. The growth becomes brownish-white in color with a more or less wrinkled, elevated surface; and microscopically the mass is found to consist in large part of the budding forms with but few mycelial threads or hyphæ.*

Freshly isolated cultures grow slightly better on *Loeffler's blood serum* than on agar media, but after the first transfer, blood serum gives no better growths than the other media. Cultures of the organism in fermentation tubes containing sugar-free broth to which 1 per cent of dextrose, levulose, saccharose, lactose, galactose, mannite, and nutrose have been added show no gas formation in any of the tubes during four weeks of observation. Freshly isolated cultures grow somewhat more readily at 37° C. than at 20° C. with a tendency to the budding form. At 20° C. the older cultures grow as rapidly as at 37° C., and the growths consist almost entirely of mycelium and aërial hyphæ. The optimum reaction of the culture media is from 0.5 per cent to 1.0 per cent acid to phenolphthalein. In agar made 0.5 per cent alkaline growth is less abundant, becoming scant at 1.5 per cent alkali and not occurring at all when higher degrees of alkalinity are employed.

ANIMAL EXPERIMENTS.

A number or guinea-pigs and rabbits were inoculated with pure cultures of the blastomyces obtained from the abscesses during life with varying results. Subcutaneous inoculations were usually followed by local abscess formation. Such abscesses as a rule contained yellowish cheesy material in which the blastomycetes were present in considerable numbers in the budding form. Even when cultures consisting chiefly of mycelium were injected, examination of the abscess after a few days showed only budding forms. In one or two cases subcutaneous injections failed to produce a typical abscess, only a slight induration remaining at the site of puncture· Likewise intraperitoneal injections of cultures were often negative no lesion whatever, being discoverable in three or four weeks after inoculation. In one rabbit, however, general miliary blastomycosis followed the intraperitoneal injection of 3 c.c. of a broth suspension of blastomyces. The organisms were demonstrated in the liver lungs, kidney, and spleen. The intravenous injection of a suspension of the blastomyces, using the marginal ear vein, resulted in two cases in rather extensive lesions in the lungs in which the blastomycetes could be demonstrated in sections. Many of the organisms were apparently undergoing degeneration and disintegration, having lost their double contour and protoplasmic granulation. Extensive hemorrhages were present in the lung tissue, and marked passive congestion in the other organs. The process seemed to be largely due to mechanical obstruction in the vessels of the lungs.

---

* The same phenomenon was observed in the case of one or two agar cultures, but we are unable to define the exact conditions under which the change took place.

In all the animal lesions, the absence of giant cells was a noticeable feature.

SUMMARY.

Etiology.—We were able to isolate from the several lesions in this case a characteristic yeastlike budding organism which morphologically and culturally belongs in the general class Oidium as defined by Ricketts, and of the several members of this group, resembles most closely the form isolated by Gilchrist and Stokes,[1] and described by them under the name *Blastomyces dermatitidis.*

The organism was repeatedly demonstrated and obtained in pure culture from the abscesses at different points and from the sputum during life. Postmortem the same organism was obtained in culture from the kidney and demonstrated in sections from the lungs, spleen, and walls of the abscess cavities, and also in pus from the abscesses, and bronchial secretion. It appeared only in the blastomycetoid form in the tissue, no sporulation nor mycelium formation being observed. When once obtained in culture it grew readily on artificial media, in both the mycelial and budding forms.

The disease was reproduced in animals by the inoculation of pure cultures of the blastomyces, and the organism again recovered postmortem from the lesions.

Finally we feel that the tubercle bacillus was definitely excluded as a causal factor in the disease. There was no family or personal history of tuberculosis. Many examinations of the sputum, urine, and pus from the abscesses by staining methods and by inoculation into guinea-pigs were made for tubercle bacilli with uniformly negative results. Examinations of smears and sections from the various organs postmortem likewise gave negative results as to tubercle bacilli.

The immediate cause of death was a terminal mixed streptococcus and staphylococcus septicemia which probably hastened death by a few days only.

---

[1] *Jour. Exper. Med.*, 1898, 3, 1, p. 53.

Clinical features.—The disease showed the characteristics of a chronic infection with gradual onset and a degree of general intoxication relatively slight when the extent of the lesions is taken into account. Diagnoses of both syphilis and tuberculosis had been made, but all who had seen the patient agreed that the case was not typical of either. On admission to the hospital, the history atypical of tuberculosis or syphilis, the number, size, and indolent character of the abscesses, and the bloody appearance of the pus suggested the probable diagnosis of generalized blastomycosis, which was at once confirmed by finding large numbers of the blastomycetes in the pus.

The infection atrium seems in all probability to have been the respiratory tract. The patient was an intelligent man, who, though engaged in manual labor, had always been unusually cleanly in his habits. He was certain that he had had no cutaneous lesions whatever previous to the appearance of the first abscess in the groin. This statement was confirmed by his wife. From his description of the succeeding lesions it seems certain that they were of the same nature as the first, and that they were due to successive localizations of the infection agent derived from some common source, probably a lesion in the lungs. It is true that during the first six months of the disease, no pulmonary symptoms were observed, but a lesion may still have been present without producing local signs, in the same way that a tuberculous focus may remain unrecognized for long periods. On admission the lungs were examined with care in view of the probability of primary pulmonary involvement, but no lesion was made out at this time. A few weeks later, however, definite pulmonary symptoms appeared together with physical signs and many blastomycetes in the sputum. It is noteworthy that the extensive pulmonary involvement found at autopsy was out of proportion to the physical findings during life.

It seems certain that dissemination of the organisms took place in very large measure, if not entirely, by the blood. The successive localizations of the blastomycetic abscesses at one point and then at another, distant from the first, the situation of the lesions chiefly on the extremities, the occurrence of miliary abscesses in the spleen, the finding of blastomycetes in sections within the blood vessels of the lung, and the absence of regional glandular involvement all speak for a condition of blastomycemia. Carefully conducted blood cultures on two occasions failed to demonstrate blastomycetes, but this is not to be wondered at when we consider the relatively large size and small number of the organisms in comparison with cases of pyemia due to bacterial infection. It is altogether likely that the organisms were carried to practically all regions of the body, but only at certain points was the local condition of the tissue such as to allow their multiplication with the formation of abscesses.

The course was progressively downward with slowly increasing anemia and emaciation. There was a constant moderate leucocytosis even when no secondary infection could be demonstrated. A slight absolute eosinophilia was present. This was observed by one of us in another case of generalized blastomycosis.

The lesions were as a rule painless except at the very beginning, when there was some tenderness over the indurated nodules. In the lesions in which the primary focus was subperiosteal the patient complained of a considerable amount of pain. In several instances the development of the small subcutaneous nodules through the successive stages of growth, softening, fluctuation, enlargement, and then rupture of the abscess, with formation of a sinus and finally a slowly healing ulcer, was observed. Where the abscesses were deep seated there was occasionally considerable dissection along the intermuscular fasciæ. Thus an abscess which formed beneath the calf muscles discharged just above the ankle, and a second abscess originating beneath the gluteal muscles pointed in the popliteal space.

Of the two superficial ulcers on the leg, it may be stated that though they showed one or two miliary abscesses at the periphery these did not contain the organisms, and the ulcers themselves were not typical of blastomycetic dermatitis. They healed uniformly from the periphery inward and apparently had resulted, as the patient stated, from the breaking-down of the skin over subcutaneous abcesses. The lesions in this case were thus practically all subcutaneous or still more deeply seated.

Anatomy.—Whenever examined, the pus from the abscesses, and later the sputum, contained the blastomycetes in considerable numbers. In some of the reported cases, it has been difficult at times to demonstrate the organisms in pus from the lesions. This was true in an unreported case seen by one of us in which there was a large subscapular abscess and a second abscess in the lumbosacral region, both containing large amounts of pus in which organisms were demonstrated only after long search. Cultures also were sterile on the first trial, and the patient left the hospital before more material could be obtained.

In the histology of the lesions a marked feature was the presence of large numbers of giant cells. This was noted particularly in the lung lesions, in which the changes were very similar to those found in acute pulmonary tuberculosis. The absence of tubercle bacilli was determined by careful search. In the lesions produced in animals, on the other hand, giant cells were not noted.

In addition to the general miliary blastomycosis of the lungs, there were several areas of ulceration with cavity formation. The present is the first case in which this has been noted. In general the distribution of the inflammatory areas in the lungs corresponded to the course of the smaller bronchi and bronchioles, and the process seemed to be true broncho-pneumonia. This fact is in accord with the view that the pulmonary infection was an inhalation process.

The superficial erosion of the vertebræ apparently followed a retroesophageal abscess and did not begin primarily in the bone.

The absence of amyloid changes in the various organs deserves mention, in view of the extensive and long-continued suppuration. This is in marked contrast to the findings in the otherwise rather similar case reported by Bassoe,[1] in which in almost all the organs amyloid changes were advanced.

---

[1] *Loc. cit.*